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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,303	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-9,13-17,19-21,25,26,67-96,104 and 107-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,13-17,19-21,25,26,67-96,104 and 107-128* is/are rejected.

7)☒ Claim(s) *25,78-80,85-96,104,108-114,126 and 127* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/2004 04/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-26, 67-96, and 104-112, in the reply filed on 31 May 2005 is acknowledged. The traversal is on the ground(s) that the election of species is "an improper attempt to restrict species within a Markush group," citing MPEP 803.02. This is not found persuasive because each sequence of a protein or nucleic acid is considered to be a patentably distinct invention for which an election is required. Accordingly, the election of broad groups, such as proteins or nucleic acids is not improper.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

3. A claim, which depends from a dependent claim, should not be separated by any claim that does not also depend from said dependent claim. In the present case claims 25, 78-80, 85-96, 104, 108-112, 126, and 127 all depend from claim 1 yet are separated from said claim 1 by independent claims 13, 67, 72, 81, and 123. Additionally, claims 113 and 114 depend from succeeding, not preceding claim 115. And multiply-dependent claim 126 is separated from independent claims 1 and 123 by independent claims 13, 67, 72, and 81, and claims 14-17, 19-21, 26, 68-71, 73-77, and 82-84, which depend therefrom. See MPEP § 608.01(n).

Specification

4. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states on numerous instances:

"These references are incorporated by reference in their entirety for all purposes."

Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents.

Attention is also directed to MPEP 608.01(p)I, which, in pertinent part, is reproduced below:

> Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. (Emphasis added)

As set forth In *Ex parte* Raible, 8 USPQ2d 1707, (BPAI, 1998)

> The examiner is of the opinion that the general incorporation by reference of the Bentley disclosure in appellant's specification is insufficient to support the specific disputed limitations of the present claims in the manner required by section 112 of the statute. We agree
>
> * * *
>
> We believe that the doctrine of incorporation by reference is of no avail to appellant in this regard since there is no specific indication in the instant specification of the particular features disclosed by Bentley which correspond to those intended for use in the here-claimed device; nor does the specification identify the specific portions of the patent which appellant may have intended to rely upon to supplement his disclosure. The purpose of incorporation by reference in an application of matter elsewhere written down is for economy, amplification, or clarity of exposition, by means of an incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found. In re de Seversky , 474 F.2d 671, 177 USPQ 144 , (CCPA 1973).

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

5. The disclosure is objected to because of the following informalities:

a. At page 91, paragraph 309, last line, there appears the expression "described described."

6. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104 and 107-128 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 is confusing as to the usage of "monomers" and "oligomers" and "fragments." As presently worded, the claims appears to require the use of "oligomers" that are in turn fragmented and "monomers" resulting therefrom are evaluated as to their mass/charge value. Said claim 1, however, also makes reference to "first number of monomers." Said usage seemingly speaks to the nucleotides/amino acids, etc., that the oligomer is comprised of, not that free monomers actually exist, however, the phrase "monomer sequences" confounds claim interpretation as monomers do not have any sequence. It is because of this apparent crossing in

nomenclature that confusion exists as to one evaluating "fragments" of "oligomers" and just how these "fragments" relate to "monomers." Claims 2-3, 25, 78-80, 85-96, 104, 109-122, 126, and. 127, which depend from said claim 1, fail to overcome this issue and are similarly rejected.

10. Similar issues exist with respect to independent claim 13, and claims 14-17, 19-21, and 26, which depend therefrom.

11. Claim 67 is confusing as to the use of the expression "non-volatile storage device." It is not clear if this expression in reference to a chemical reactor or to a computer memory.

12. Claim 77 is indefinite with respect to what constitutes the metes and bounds of "L1 or L2 cache."

13. Claim 78 is confusing with respect to what is the "abundance value" determined.

14. Claim 81 is indefinite as a result of the term "might." Said claim 81 is confusing as to the use of the phrase "monomer length." Seemingly a monomer is just that, a monomer, and is without "length" as there is but a single unit. Similarly, there cannot be a "monomer sequences." Claims 82-84, which depend from said claim 81, fail to overcome this issue and are similarly rejected.

15. Claim 87 is confusing as to what constitutes "a reducing terminus" as the means of reducing are not defined.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

18. Page 18, paragraph 70, of the disclosure provides the following definitions.

[0070] As used herein, the term "oligomer" refers to any polymer of residues wherein the residues are similar, though typically not identical. Generally, an oligomer is meant to include naturally-occurring polymers such as proteins, oligonucleotides, nucleic acids, oligosaccharides, polysaccharides, lipids, and the like. Oligomer may also refer to free radical, condensation anionic or cationic polymers of synthetic origin, which include, but are not limited to acrylates, methacrylates, nylons, polyesters, polyimides, nitrile rubbers, polyolefins, and block or random copolymers of different monomers in these classes of synthetic polymers. The oligomer that is subject to the analytical methods described herein will have a number of residues that are typical of their naturally occurring number. For example, and oligomer that is an oligonucleotide may have hundreds and even thousands of residues. Similarly, a protein will generally have one hundred or more residues (though the sequencing of smaller fragments, e.g. peptides is also useful). An oligosaccharide will typically have from 3 to 100 sugar residues. A lipid will normally have 2 or 3 fatty acid residues. 18

19. While a restriction has been placed against the claims, and applicant has elected the oligomer of "protein," there is no upper limit to the number of amino acid residues of which the "protein" is comprised. And there is virtually no limit to the type and number of compounds to be considered as encompassed by the term "oligomer."

20. A review of the disclosure finds the following examples:

b. Example 1, pages 69-72, drawn to the detection of linked mannoses.

c. Example 2, pages 72-74, directed to identification of fatty acid composition and arrangement in lipids as found in the bacteria *E. coli*.

d. Example 3, pages 75-77, drawn to the preparation of photocleavable mass defect labels of the brominated or iodinated aryl ether variety.

e. Example 4, pages 77-80, demonstrates use of affinity-coupled mass labels, e.g., iminobiotin affinity tag.

f. Example 5, pages 80-82, drawn to incorporating bromophenylamide derivatives of amino acids

g. Example 6, page 83, "shows the utility of the photocleavable mass defect labels generated in Example 5."

h. Example 7, page 84, "illustrates the conjugation of a mass-defect label, the N-hydroxysuccinimide (NHS) ester of 5-bromonicotinic acid, to horse apomyoglobin (Myo).

i. Example 8, pages 84-85, "illustrates the generation of sequencing mass spectral fragment ion species from 5-BrNA labeled myoglobin by IMLS that are shifted from the periodic chemical noise."

j. Example 9, pages 86-87, "illustrates the conjugation of a mass-defect label, N-hydroxysuccinimide (NHS) ester of 5-bromo-3-pyridylacetic acid (5-Br-3-PAA), to horse apomyoglobin (Myo)."

k. Example 10, page 87, "illustrates the use of the automated deconvolution and sequencing algorithms of this invention to find the N-terminal sequence of 5-Br-3-PAA labeled myoglobin fragmented in-source in an ESI-TOF mass spectrometer.

l. Example 11, pages 87-88, "illustrates the synthesis of a generic mass-defect label that incorporates a mass-defect element of this invention (i.e., bromine), an ionizable group (i.e., pyridyl) and a succinic anhydride linking moiety for attachment to the N-

terminus or other desired primary or secondary amino group of a peptide or other species."

m. Example 12, pages 88-91, "illustrates the use of mass defect labels in DNA sequencing applications."

n. Example 13, page 91, "the mass defect label (5-Br-3-PAA) [is used] to sequence bovine ubiquitin (Sigma-Aldrich)." As stated therein

The correct sequence ranked second out of 19 competing possibilities at the first residue. The correct sequence was also ranked second (to MQIFR) at the fifth residue.

21. Example 13 relates most closely to the elected invention. As seen therein, the method did not result in the first choice of the 19 possible amino acids actually comprising the correct sequence. The disclosure fails to provide an adequate written description of just how one would reproducibly identify the correct amino acid sequence of numerous proteins when the correct amino acid sequence is unknown, or may have a point mutation.

22. The specification is essentially silent as to how one would identify, in a reproducible manner, the correct sequence of residues of any polymer, be it a polypeptide of not. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

23. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

24. Claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co.*,

Ltd., 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

25. As set forth above, the specification does not provide an adequate written description of the invention so as to reasonably suggest that applicant as in possession of the invention at the time of filing. It is well settled that one cannot enable that which they do not yet possess. Accordingly, claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

26. The claims have been interpreted as encompassing the correct and reproducible sequencing of any and all manner of polymers. As set forth in paragraph 70 of the original disclosure (and reproduced in paragraph 18 above), the form of the oligomer envisaged by applicant is truly quite diverse. While one is not required to teach in exhaustive detail each and every embodiment encompassed by the claims, the specification still must fully enable the scope of that being claimed. As seen above, Example 13 is most closely related to the elected invention. The specification readily admits that the first choice of the predicted amino acid residues was not the correct amino acid sequence. If not for the fact that applicant was using a known control, the degree of inaccurate measurement/predicting would not have been known. The specification does not teach how one would correctly identify the correct sequence of any oligomer, be it a polypeptide or some other polymer, when the correct sequence is unknown. Further, the specification is essentially silent as to how one would identify the correct order of sequence of an oligomer when the oligomer (e.g., polypeptide) has point mutations, inversions, or even truncations.

27. While the specification does contain numerous examples, those examples, however, have not been found to set forth the specific reaction conditions and essential starting materials so to fully enable the claimed methods. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

For the above reasons, and in the absence of convincing evidence to the contrary claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Conclusion

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

29. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
26 November 2005